



EP1654

PATENT APPLICATION  
Docket No.: DUK96-03pA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jonathan S. Stamler  
Application No.: 08/616,371 Group: 1654  
Filed: March 15, 1996 Examiner: B. Celsa  
For: Methods for Producing and Using S-Nitrosohemoglobins

CERTIFICATE OF MAILING

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INTERVIEW SUMMARY

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Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

On August 5, 1999, an interview was conducted at the United States Patent and Trademark Office. Carol A. Egner and David E. Brook (Attorneys of Record) and Jonathan S. Stamler, M.D. (Applicant) discussed the application with Bennett Celsa (Patent Examiner). Related applications 08/667,003 filed June 20, 1996, 08/796,164 filed February 6, 1997 and 08/874,992 filed June 12, 1997 were also discussed during the same interview.

At the time of filing a Brief On Appeal, on June 7, 1999, Claims 1-3 and 6-8 had been canceled; Claims 4, 5, 9-14, 28 and 29 had been allowed; Claims 15-27 had been finally rejected and were the subject of the Brief on Appeal. At the interview, Mr. Celsa indicated that the application would be withdrawn from appeal and prosecution reopened. The Stamler *et al.* published PCT patent application WO 93/09806 was discussed as it affects the claims.

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WO 93/09806 was the subject of a Declaration of Jonathan S. Stamler, M.D. Under 37 C.F.R. § 1.132 mailed to the United States Patent and Trademark Office on February 27, 1998, and a Declaration of Joseph Bonaventura, Ph.D. Under 37 C.F.R. § 1.132 mailed to the United States Patent and Trademark Office on March 12, 1998. It was explained to Mr. Celsa that Example 19 of WO 93/09806 and Example 1 of U.S. Patent Application No. 08/559,172 (abandoned as of July 6, 1999), both purporting to describe a procedure resulting in the synthesis of SNO-hemoglobin, both arose from the same set of experiments performed by Dr. Stamler, even though the accounts of those experiments in the Examples differed in details of the procedure, and both were, in fact, inaccurate in some aspects.

Dr. Stamler elaborated on the statements presented in his Declaration of February 27, 1998. He explained that the experiment resulting in the spectrum of Figure 28 of WO 93/09806 and Figure 1 of 08/559,172 employed acidified nitrite as the reagent. Although the assay to detect SNO-hemoglobin had been done incorrectly, even had the assay been performed correctly, the products were dissociated hemes and dissociated, denatured subunits. Similar treatment of more acid resistant proteins had resulted in the production of *S*-nitrosoproteins. Figure 29 of WO 93/09806 (Figure 2 of 08/559,172) shows the result of an experiment in which *S*-nitroso-N-acetylcysteine (SNOAc) was added to hemoglobin. Although the description in the Examples recites a different conclusion, the correct conclusion apparent to one of skill in the art is that the spectrum shows that the product contains oxidized hemoglobin, methemoglobin.

As was explained in item 5 of the Declaration of Dr. Stamler, the experimental conditions one might conclude from the Examples were used in an attempt to synthesize SNO-hemoglobin, were tried in more recent experiments in Dr. Stamler's laboratory. Using 12.5  $\mu$ M SNOAc and 12.5  $\mu$ M hemoglobin at pH 6.9 did not produce detectable SNO-hemoglobin. See Exhibits E1-E3 with the Declaration of Dr. Stamler.

Mr. Celsa will be reconsidering the prior art and how it may affect the claims. Mr. Celsa also raised some concerns about the scope of the claims. Claim language was not specifically discussed.

Respectfully submitted,

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